Psoriatic Arthritis: The Need for Early Intervention

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**ABSTRACT.** About 30% of individuals with skin psoriasis will develop an inflammatory disease of the peripheral or axial skeleton involving synovial and/or entheseal tissue termed psoriatic arthritis (PsA). In most cases psoriasis will precede PsA by several years. Hence skin psoriasis provides an opportune model to investigate genetic and environmental factors that interact and contribute to the development of a common form of inflammatory arthritis. Further, the preexisting presence of psoriasis represents a unique opportunity for the early detection of arthritis and the potential for more effective intervention. However, despite the presence of psoriasis, there may be delay in the diagnosis of PsA that is associated with adverse longterm outcome. Undiagnosed disease is not uncommon, as demonstrated by studies applying screening questionnaires to primary care and dermatology clinic populations. Other potential risk factors, such as obesity and smoking, the presence of certain genetic and biomarker profiles, combined with accurate imaging modalities, offer the potential for more targeted screening. So in future it should be possible to detect PsA at a much earlier stage and prevent significant joint damage and associated disability before it happens. (J Rheumatol Suppl. 2015 Nov; 93:10–13; doi:10.3899/jrheum.150625)

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Verna Wright Lecture

The concept of psoriatic arthritis (PsA) owes much to the insightful studies of Verna Wright. In one of his earliest studies 42 cases of psoriasis with arthritis were described and compared with 55 unselected patients with rheumatoid arthritis and 310 patients with psoriasis alone. He concluded that most of the 42 cases comprised a distinct entity. Of interest he was surprised by finding nail changes in 4 male patients with osteoarthritis, although possibly he may have been witnessing the bony proliferative element of PsA we recognize today. Notwithstanding he was the first to document the topographical association between nail disease and distal interphalangeal joint disease. In a later article he demonstrated many of the characteristic radiological features of PsA such as osteolysis and a greater incidence of sacroiliac joint change. His conclusion that PsA was “less severe than rheumatoid arthritis” is somewhat more contentious, but most certainly his observations of the different phenotypes of PsA were landmark findings.

We now recognize that PsA is not a benign condition, and with more effective treatments available there may never be a better opportunity for preventing its development from an early stage. Skin psoriasis precedes the development of PsA in the majority of cases and so represents an excellent opportunity for implementing screening strategies. Some of the evidence for the importance of early detection will be reviewed, as will recent epidemiological findings, the development of screening questionnaires, and identification of high-risk groups where screening should be applied. The review is not comprehensive and concentrates on selective recent findings.

Is PsA Underdiagnosed?

Published estimates of the incidence and prevalence of PsA have varied, most likely due to the type of study setting, differences in the method of case ascertainment, and developments in diagnostic or classification criteria, such as the more recent adoption of the CASPAR (ClASsification for Psoriatic Arthritis criteria). A systematic review reported a median incidence of 6.4/100,000 cases per year of PsA in the general population, yet a more recent population-based study from Norway found 188 incidence cases over an 8-year period giving an incidence rate of 41.3/100,000. In a longitudinal retrospective population-based study of psoriasis using a medical records-linked system, there was a 10-year cumulative incidence of 3.1% in Olmsted County, Minnesota, USA. In contrast, a prospective cohort study of psoriasis in Toronto, Canada, reported a higher incidence of 1.8%. However, both incidence and prevalence of PsA may be even higher. Studies using screening questionnaires applied to psoriasis populations in dermatology and primary care settings have revealed that many patients are undiagnosed. In a German study there were 10.9% of patients from dermatology clinics with undiagnosed PsA and as many as 29%
in a study from Dublin. Although retrospective studies do point to the potential importance of early diagnosis, it is important to note that the natural history of undiagnosed PsA is unknown.

**Observational Studies of Outcome in PsA**

Long-term observational studies of PsA have provided valuable information on the natural history of PsA. Health-related quality of life measures are affected in a degree similar to rheumatoid arthritis. An atherogenic lipid profile is associated with active PsA, there is an increased incidence of subclinical atherosclerosis, and an increased risk of cardiovascular disease. Joint damage occurs in 47% of patients within 2 years of disease onset.

Several studies of longitudinal disease cohorts suggest that delay in diagnosis is associated with a worse outcome. In the Toronto cohort a greater rate of joint damage was reported in those patients first seen after 2 years of disease compared to those seen within 2 years. In our own Bath cohort, delay in diagnosis, smoking, female gender, and older age at onset were associated with a worse physical function measured by the Health Assessment Questionnaire (HAQ) after 10 years. Similar observations were reported in a Dublin cohort with late consulters having greater peripheral joint erosion and worse physical function. In a prospective study from the Swedish Early PsA Register a shorter duration of symptoms and lower HAQ scores were independent predictors of reaching a state of minimal disease activity at 5 years. Therefore there is increasing evidence that early intervention may be important in reducing the burden of disease, although further prospective studies are needed.

**Detection of Early Disease**

**Screening questionnaires.** There have been several questionnaires available to screen for patients with PsA in various settings. The performance of the questionnaire has been compared in several studies, such as 2 comparing the PASE (Psoriatic Arthritis Screening Evaluation): the Toronto Psoriatic Arthritis Screen (ToPAS) and the Psoriasis Epidemiology Screening Tool (PEST); and another: PASQ (Psoriasis and Arthritis Screening Questionnaire) with ToPAS and PEST. In general the screening tools help identify a substantial number of patients with undiagnosed PsA and patients who may benefit from rheumatology review. A further questionnaire [Comparison of Three Screening Tools for psoriatic arthritis (CONTEST)] has been derived, combining optimal questions from existing tools, and needs further evaluation. Questions remain regarding the appropriate healthcare setting in which to apply the questionnaires, the frequency of their use, and the characteristics of the target population. Also patients with PsA may have mild psoriasis that never comes to healthcare attention until after PsA is diagnosed and so they may not be captured by screening.

**Imaging.** Imaging studies have revealed preclinical disease in patients with psoriasis alone. Indeed patients with psoriasis clinically asymptomatic for musculoskeletal disease have a higher prevalence of enthesial abnormalities on ultrasound than age- and sex-matched controls. Power Doppler may detect vascular changes that distinguish PsA from psoriasis alone and offers the potential for detecting early development of arthritis. Psoriasis patients with nail changes had higher enthesis scores at remote sites than patients with normal nails, consistent with observations that patients with PsA have a greater frequency of nail disease than psoriasis patients alone. MRI scanning may reveal subclinical synovitis and enthesitis in patients with psoriasis without arthritis symptoms.

**Risk Factors for PsA in Psoriasis**

**Clinical and lifestyle.** There are relatively few studies addressing the pattern of psoriasis as a risk factor for PsA. One such study found that scalp and intergluteal psoriasis and nail disease put those individuals at risk of developing PsA. Nail disease is more common in patients with PsA compared to psoriasis and has been confirmed as a risk factor in a more recent study. Evidence for smoking as a risk factor is more conflicting, with at least 2 studies finding smoking a positive risk factor and another reporting that smoking is protective. A population-based study using The Health improvement Network (THIN) database reported a greater incidence rate of PsA in a psoriasis population with increasing body mass index. At least 1 study has reported the prevalence of PsA to be associated with greater extent of psoriasis and low PASI scores. Although the median time of onset of PsA is within 10 years of onset of psoriasis, notably 1 study of European dermatology centers found the incidence rate of PsA remained constant with time following the diagnosis of psoriasis.

**Genetic factors.** There are genetic susceptibility factors common to both psoriasis and PsA. However, some known genetic factors such as presence of the HLA-Cw6 allele are strongly associated with psoriasis and more so in younger patients than in PsA itself. Therefore, there likely exist genetic factors associated with susceptibility to PsA other than those for skin psoriasis alone. Three such loci appear to be interleukin 13, HLA-B27, and PTPN22. The presence of HLA-B27 is associated with a shorter interval between the onset of psoriasis and the onset of PsA. Further, different combinations of HLA-B and HLA-C alleles and haplotypes may be associated with particular phenotypes and disease severity.

**Other biomarkers.** Osteoclast precursors are upregulated in PsA and can be identified by cellular markers such as dendritic cell-specific transmembrane protein (DC-STAMP). There are data to suggest that patients with psoriasis who develop arthritis show increased DC-STAMP expression on peripheral blood mononuclear cells. Measurement requires freshly isolated cells and access to flow cytometry and so is
not at present a feasible strategy for screening. Other soluble biomarkers that can be more readily measured are of interest, and bone turnover markers have been the subject of a recent systematic review. Markers that appear to differentiate PsA from psoriasis include matrix metalloproteinase-3, dickkopf 1, macrophage colony stimulating factor, a ratio of type II collagen synthesis to degradation, and possibly osteoprotegerin. Increased levels of highly sensitive C-reactive protein may also be discriminatory. These markers need further study in a prospective cohort of patients with psoriasis to test their predictive value.

In conclusion, the longterm outcome of PsA in those patients referred to a rheumatology service carries a high disease burden. Less is known of the outcome in patients who do not seek medical attention or who remain undiagnosed. The estimated mean health cost is high, especially in those with severe loss of physical function. There are high levels of unemployment and loss of productivity that may be more readily reversible with early intervention. With the development of treat-to-target regimes using more effective therapies the case for early intervention is even stronger. Individuals with psoriasis who would appear to be at most risk are those who are obese, have nail disease, and carry the HLA-B27 allele. However, more knowledge is needed to create robust bioprofiles that can be applied to clinical phenotypes that stratify patients into appropriate treatment pathways and help implement effective screening strategies.

REFERENCES


